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Ivonescimab plus chemotherapy versus durvalumab plus chemotherapy as first-line treatment for advanced biliary tract cancer: A randomized, controlled, double-blinded, phase 3 trial (HARMONI-GI1)

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Background

Durvalumab plus chemotherapy (chemo) is the standard first-line treatment for advanced biliary tract cancer (BTC). In the current phase 3 study conducted in China, we evaluated the efficacy and safety of ivonescimab, a PD-1/VEGF bispecific antibody, plus chemo versus durvalumab plus chemo as first-line treatment for advanced BTC. Here we report the results from the preplanned interim analysis.

Methods

Eligible patients with unresectable locally advanced or metastatic BTC were stratified by disease status (locally advanced vs. metastatic) and primary tumor location (intrahepatic cholangiocarcinoma vs. extrahepatic cholangiocarcinoma vs. gallbladder cancer), and randomized 1:1 to receive ivonescimab or durvalumab plus gemcitabine and cisplatin (Q3W, 8 cycles), followed by ivonescimab or durvalumab maintenance therapy. The primary endpoint was overall survival (OS). Key secondary endpoints included progression-free survival (PFS) and objective response rate (ORR).

Results

682 patients were randomized (ivonescimab: 340; durvalumab: 342). Baseline characteristics were balanced between arms. Median follow-up was 14.3 months. The primary endpoint was met. Median OS was significantly improved with ivonescimab plus chemo versus durvalumab plus chemo (14.9 vs. 12.1 months; HR 0.75, 95% CI 0.61-0.92, P = 0.0031). Median PFS was 8.4 vs. 5.8 months (HR 0.61, 95% CI 0.51-0.72, P < 0.0001). The ORR was 53.8 % vs. 32.5 % (P < 0.0001). Treatment-related adverse events were generally well tolerated, with a manageable safety profile. The most common treatment-emergent adverse events (TEAEs) were haematological toxicity. No new safety signals were identified for ivonescimab.

Conclusions

Ivonescimab plus chemo significantly improved OS, PFS and ORR in patients with advanced BTC compared with durvalumab plus chemo, with a manageable safety profile. These results support ivonescimab plus chemo as a potential new first-line standard of care for advanced BTC.

Clinical trial identification

NCT06591520.

Legal entity responsible for the study

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Disclosure

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